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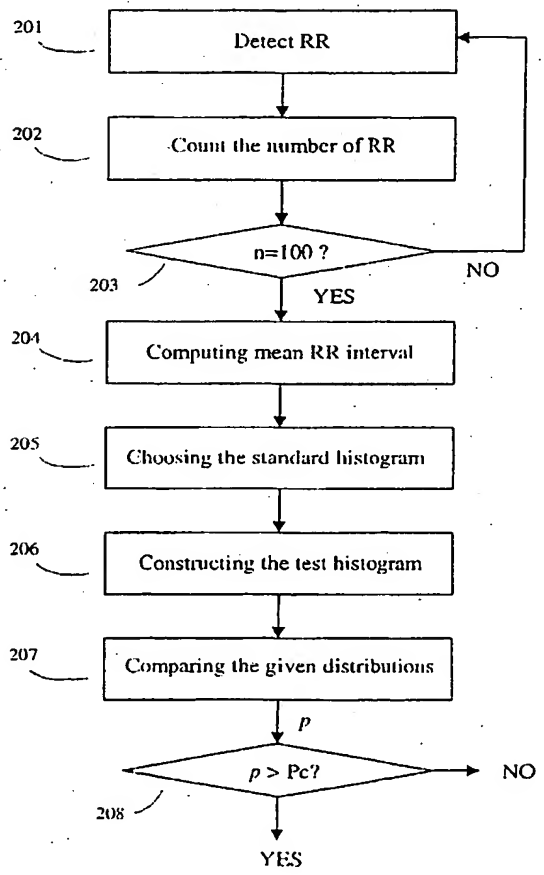
(54) Title: METHOD AND SYSTEM FOR DETECTION OF CARDIAC ARRHYTHMIA



(57) Abstract: There are many different serious cardiac arrhythmias. The present invention uses measurements of RR intervals (interbeat intervals) to detect, in particular but not exclusively, atrial fibrillation of a patient. Atrial fibrilation is a serious ailment in which the heartbeat is generally rapid and irregular. Probability density histograms of ΔRRs (difference between two successive RR intervals) collected during atrial fibrillation of a plurality of subjects are used as a template for the detection of atrial fibrillation. In one implementation, there are 16 standard probability density ΔRRs histograms every 50 ms of mean RR interval of a certain number of beats, where the mean RR interval ranges from 350 ms to 1149 ms. Similarity between the standard probability density histograms and a test density probability histogram of ΔRRs of a patient is estimated by the Kolmogorov-Smirnov test. If the test density histogram is not significantly different from the standard density histogram, atrial fibrillation is detected.

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METHOD AND SYSTEM FOR DETECTION OF CARDIAC ARRHYTHMIA

BACKGROUND OF THE INVENTION

1. Field of the invention:

The present invention relates to a method and a system for detecting cardiac arrhythmias from internally and/or externally detected activity of the heart .

2. Brief description of the prior art:

Atrial fibrillation is a serious and common cardiac arrhythmia. Atrial fibrillation is associated with rapid, irregular atrial activation with life threatening sequelae such as stroke. The atrial activations are irregularly transmitted through the atrioventricular node leading to a correspondingly irregular sequence of ventricular activations as monitored by the ventricular interbeat (RR) intervals on the surface electrocardiogram (ECG). An RR interval is an interval between two successive heart beats. Clinically, in the surface ECG, atrial fibrillation is diagnosed by absence of P waves (normally associated with the near synchronous activation of the atria) and a rapid irregular ventricular rate. P waves are difficult to determine automatically and irregular baseline activity of the ECG is common in atrial fibrillation.

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Although a number of different methods have been proposed to test for atrial fibrillation based on knowledge of the RR intervals and/or the surface ECG, the detection of atrial fibrillation based on this data nevertheless poses substantial problems (Murgatroyd, et al. "Identification of Atrial Fibrillation Episodes in Ambulatory Electrocardiographic Recordings: Validation of a Method for Obtaining Labeled R-R Interval Files," Pacing and Clinical Electrophysiology, (1995), pp.1315-1320). In the following description, the main strategies that have been proposed to assess atrial fibrillation based on knowledge of the RR intervals and/or ECG will be briefly reviewed.

Since RR intervals during atrial fibrillation have a larger standard deviation and a more rapid decay of the autocorrelation function, there are proposals that the standard deviation and the autocorrelation function can be used to distinguish atrial fibrillation from sinus rhythm (Bootsma, et al. "Analysis of RR Intervals in Patients with Atrial Fibrillation at Rest and During Exercise," Circulation, (1970), pp.783-794). Since other abnormal rhythms also have a large standard deviation of RR intervals and a rapid decay of the autocorrelation function, these methods are difficult to apply in concrete situations.

Moody and Mark (G. Moody, et al. "A New Method for Detecting Atrial Fibrillation Using R-R Intervals," Computers in Cardiology, (1983), pp.227-230) classify RR intervals as short, long or regular. They then construct a Markov model for the probabilities for transitions between RR intervals in each of the three different length classes. Atrial fibrillation data has typical transition probabilities not shared by normal rhythms or other arrhythmia. Although the Markov model has high sensitivity for detecting atrial fibrillation, it tends to have a relatively low predictive value of a positive test.

Pinciroli and Castelli have investigated the morphology of histograms of RR intervals collected during atrial fibrillation and other arrhythmia (F. Pinciroli, et al. "Pre-clinical Experimentation of a Quantitative Synthesis of the Local Variability in the Original R-R Interval Sequence in the Presence of Arrhythmia," Automedica, (1986), vol.6, pp.295-317.Pinciroli and Castelli, 1986). They demonstrated that the histograms of the ratio between successive RR intervals show characteristic differences between normal rhythm and atrial fibrillation. The histogram of the ratio between successive RR intervals is symmetrical to the mean value. No quantitative methods were proposed to quantify the symmetry or to use it to develop a quantitative test.

Since the baseline of the ECG is irregular during atrial fibrillation, Slocum (J. Slocum, et al. "Computer Detection of Atrial Fibrillation on the Surface Electrocardiogram," Computers in Cardiolody, (1987), pp.253-254) has proposed that the regularity of the baseline, as determined by the power spectrum of the residual ECG after subtraction of the baseline of the QRS complexes can be used to detect atrial fibrillation. This method is necessarily sensitive to small amounts of noise that might corrupt the baseline of the ECG.

Implantable ventricular and atrial defibrillators are devices that distinguish atrial and ventricular fibrillation from other rhythms. Typically, electrodes in these devices record intracardiac activity directly from the atria and ventricles. The methods that are used to detect atrial fibrillation in these devices cannot be easily applied to recordings that give information about the timing of the QRS complexes (U.S. Pat. No. 6,144,878, issued to Schroeppel on November 7, 2000, U.S. Pat. No. 6,035,233 issued to Schroeppel on March 7, 2000, U.S. Pat. No.

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5,749,900 issued to Schroeppel on May 24, 1998, U.S. Pat. No. 6,064,906 issued to Langberg et al. on May 16, 2000, U.S. Pat. No. 5,772,604 issued to Langberg et al. on June 30, 1998, U.S. Pat.No. 6,061,592 issued to Nigam on May 9, 2000, U.S. Pat. No. 5,951,592 issued to Murphy on September 14, 1999, U.S. Pat. No. 5,941,831 issued to Turcott on August 24, 1999, U.S. Pat. No. 5,591,215 issued to Greenhut et al. on January 7, 1997).

Analysis of a histogram of the interbeat intervals can be used to discriminate between ventricular fibrillation and ventricular tachycardia. By counting the number of beats in predetermined interval classes, an algorithm identifies a given sequence as ventricular fibrillation or ventricular tachycardia (U.S. Pat. No. 5,330,508 issued to Gunderson on July 19, 1994). While this patent suggests that the invention is of value in detecting and treating atrial fibrillation (column 2, lines 29-31), it does not provide specific embodiment for detecting and treating atrial fibrillation.

Based on the foregoing review of the prior art, it is apparent that there is a need to develop a method and a system for determining whether or not a given recording is atrial fibrillation based on the timing of the QRS complexes as measured from an internal and/or external monitor. Assessment of whether a patient is in atrial fibrillation based on the timing of the QRS complexes would be extremely useful, for example, for assessing the efficacy of specific drugs on a patient fitted with a monitoring device that measures the timing of the QRS complexes.

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SUMMARY OF THE INVENTION

In accordance with the present invention there is provided a method for detecting cardiac arrhythmia of a patient, comprising detecting RR intervals of the patient wherein each RR interval is an interval between two heart beats, constructing standard histograms of ΔRRs collected during cardiac arrhythmia of a plurality of subjects wherein each ΔRR is a difference between two successive RR intervals, constructing test histograms of ΔRRs of the patient from the detected RR intervals of this patient, and comparing the standard and test histograms to detect whether the patient suffers from cardiac arrhythmia.

In accordance with preferred embodiments:

- the standard and test histograms are probability density histograms;
- a mean value of a given number of successive RR intervals of the patient is calculated, and a standard probability density histogram is chosen in relation to this mean value;
- the comparison of the standard and test histograms comprises adjusting a specificity-altering and sensitivity-altering parameter;
- the comparison of the standard and test histograms comprises:
  - calculating a standard cumulative probability distribution from the standard ΔRR probability density histograms;
  - calculating a test cumulative probability distribution from the test ΔRR probability density histograms;

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- computing a deviation between these standard and test distributions; and
- detecting cardiac arrhythmia when the computed deviation is higher than the specificity-altering and sensitivity-altering parameter.

The present invention also relates to a system for detecting cardiac arrhythmia of a patient, comprising:

an RR interval detecting monitor detecting RR intervals of the patient, wherein each RR interval is an interval between two heart beat;

a standard ΔRR histogram storage unit in which are stored standard histograms of ΔRRs collected during cardiac arrhythmia of a plurality of subjects, wherein each ΔRR is a difference between two successive RR intervals;

a test ΔRR histogram calculator supplied with the detected RR intervals from the monitor and constructing test histograms of the ΔRRs of the patient; and

a standard and test ΔRR histograms comparator supplied with the standard and test histograms, this comparator comprising a detector of cardiac arrhythmia of the patient responsive to the comparison of the standard and test histograms.

It is within the scope of the present invention to apply the above concept to detection of not only atrial fibrillation but also to other cardiac arrhythmias including in particular but not exclusively atrial flutter, multifocal atrial tachycardia, ventricular tachycardia, premature ventricular contractions, etc., as well as to detection of other body phenomenon involving electrical activity. It is also within the scope of the present invention to use signals other than the RR intervals, histograms other than ΔRR probability density histograms, tests other than the KS test, and

series of ΔRRs other than 100, and that other methods besides the Komogorov-Smirnov test can be used to compare test histograms with the standard histograms.

The foregoing and other objects, advantages and features of the present invention will become more apparent upon reading of the following non restrictive description of a preferred embodiment thereof, given by way of example only with reference to the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

In the appended drawings:

Figure 1 are time series showing the RR intervals from subject 202 from the MIT-BIH arrhythmia database. The solid line directly under the time series of RR intervals shows the assessment of atrial fibrillation (indicated by AF) or non-atrial fibrillation (indicated by N) as reported in the database. The solid line at the bottom of Figure 1 indicates the assessment of atrial fibrillation, indicated by 1, and non-atrial fibrillation, indicated by 0, based on an algorithm presented herein.

Figure 2 is a flow chart illustrating a preferred embodiment of the method according to the present invention, for detecting atrial fibrillation based on RR intervals.

Figure 3a-3p are ΔRR standard probability density histograms during atrial fibrillation. Mean RR intervals are a) 350-399 ms, b) 400-449

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ms, c) 450-499 ms, d) 500-549 ms, e) 550-599 ms, f) 600-649 ms, g) 650-699 ms, h) 700-749 ms, i) 750-799 ms, j) 800-849 ms, k) 850-899 ms, l) 900-949 ms, m) 950-999 ms, n) 1000-1049 ms, o) 1050-1099 ms, and p) 1100-1049 ms.

Figure 4 is the standard deviation of ΔRR which consists of the standard ΔRR probability density histogram as a function of mean RR interval.

Figure 5 illustrates the Kolmogorov-Smirnov (KS) test. A cumulative probability distribution based on patient test data is compared with a standard cumulative probability distribution. *D* is the greatest distance between two cumulative probability distributions.

Figures 6a and 6b show an example of the standard deviation (Figure 6a) and the skewness (Figure 6b) of a test ΔRR probability density histogram. The line represents the standard deviation (Figure 6a) and the skewness (Figure 6b) of the standard ΔRR probability density histogram.

Figure 7 shows the receiver operating characteristic curve (ROC) when this method is tested on the MIT-BIH atrial fibrillation/flutter database. The specificity increases with increase in P_c, while the sensitivity decreases with an increase in P_c.

Figure 8 is a block diagram of a preferred embodiment of the system according to the present invention for implementing the method of Figure 2, for detecting atrial fibrillation based on RR intervals.

Figure 9 is a block diagram of a preferred embodiment of a test and standard ΔRR histogram comparator forming part of the system of Figure 8.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Although the preferred embodiment of the present invention will be described in relation to atrial fibrillation, the same concept can be applied to detection of other cardiac arrhythmias including in particular but not exclusively atrial flutter, multifocal atrial tachycardia, ventricular tachycardia, premature ventricular contractions, etc. This concept can also be applied to detection of other body phenomenon involving electrical activity.

Data was obtained from the MIT-BIH atrial fibrillation/flutter *database. The data contains 300 atrial fibrillation episodes, sampled at* 250 Hz for 10 hours from Holter tapes of 25 subjects. Arrhythmia detection was carried out by trained observers and was confirmed by an independent evaluation.

Figure 1 is a typical time series of RR intervals from a patient with *atrial fibrillation. Immediately under the recording is a solid marker line* 101. When atrial fibrillation occurs this marker line 101 is set to AF; otherwise it is set to N, which indicates a rhythm that is not atrial fibrillation. The graph of Figure 1 also shows a lower solid line 102 indicating the assessment of atrial fibrilation, indicated by 1, and non-atrial fibrilation, indicated by 0, based on an algorithm according to the present invention. At the onset of atrial fibrillation, the rhythm dramatically

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changes to irregular with large fluctuation. In paroxysmal atrial fibrillation there is sudden starting and stopping of atrial fibrillation.

Figure 2 shows a flow chart of a preferred embodiment of the method according to the invention for detecting atrial fibrillation. Figure 8 is a block diagram of a preferred embodiment of the system according to the invention for implementing this method.

The standard ΔRR probability density histograms are prepared as described hereinafter before the detection of atrial fibrillation, and then stored in an adequate storage unit 804 (Figure 8).

RR intervals of the patient are first detected (201 of Figure 2) through an internal and/or external RR interval monitor 801 (Figure 8) detecting electrical activity of the heart beat of the patient.

ΔRR is defined as the difference between two successive RR intervals. In the preferred embodiment, blocks of 100 successive RR intervals are processed during atrial fibrillation. For that purpose, the detected RR intervals from the monitor 801 are counted (202 of Figure 2) by a RR interval counter 802 (Figure 8) until the number of detected RR intervals reaches 100 intervals (203 of Figure 2).

The mean value of each block of 100 RR intervals is computed (204 of Figure 2) by means of a calculator 803 from the RR intervals from the monitor 801. Of course, the calculator 803 is supplied with the count from the counter 802. This mean value identifies the block of 100 RR intervals as falling into one of sixteen (16) different classes, respectively corresponding to mean values of RR between 350-399 ms, 400-449 ms, 450-499 ms, 500-549 ms, 550-599 ms, 600-649 ms, 650-699 ms, 700-

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749 ms, 750-799 ms, 800-849 ms, 850-899 ms, 900-949 ms, 950-999 ms, 1000-1049 ms, 1050-1099 ms, and 1100-1049 ms. For each of the sixteen (16) classes, a standard ΔRR probability density histogram is compiled by lumping data together from all the subjects, for example the subjects of the above mentioned MIT-BIH atrial fibrilation/flutter database. The resulting histograms (see for example in Figures 3a-3p) are taken to be the standard ΔRR probability density histograms for atrial fibrillation, sorted by the mean RR interval (see for example in Figures 3a-3p) and stored in storage unit 804. In other words, a standard ΔRR histogram selector 805 chooses the standard ΔRR probability density histogram (Figures 3a-3p) corresponding to the class in which the computed mean value of RR intervals (from 204 in Figure 2) of the block of 100 RR intervals under consideration falls (205 of Figure 2).

Obviously, it is within the scope of the present invention to construct the standard ΔRR probability density histograms using a different number of consecutive RR intervals, for example 25, 50 or any other number of consecutive RR intervals. It is also within the scope of the present invention to construct the standard ΔRR probability density histograms using mean RR intervals that lie in other ranges, for example 300-399 ms, 400-499 ms, 500-599 ms, etc.

Figure 4 shows the standard deviation (SD) of the standard probability density histograms of ΔRR.

Test ΔRR probability density histograms are constructed (206 of Figure 2) by a calculator 806 from the data obtained from the patient (test record) through the monitor 801. As indicated in the foregoing description, the blocks of 100 successive RR intervals are determined by the counter 802. In order to test for atrial fibrillation in a test record, the test ΔRR

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probability density histograms based on the blocks of 100 successive RR intervals from the test record, are compared (207 and 208) through a comparator 807 to the chosen standard ΔRR probability density histograms from selector 805.

In the test ΔRR histogram calculator 806 a sequence of 100 RR intervals is centered on each beat in turn, and the relevant test ΔRR probability density histograms are calculated. Also, a standard cumulative probability distribution is calculated by integrating the area under the curves of the standard ΔRR probability density histograms, and a test cumulative probability distribution is computed by integrating the area under the curves of the test ΔRR probability density histograms (Figure 5).

The similarities between the test histograms for a given patient and the standard histograms are evaluated in the test and standard ΔRR histogram comparator 807 using the above mentioned Kolmogorov-Smirnov (KS) test (207 and 208 of Figure 2). As indicated, Figure 5 shows an example of cumulative probability distributions of standard histograms (standard curve) and test histograms (test curve).

Referring to Figure 9, a calculator 901 (Figure 9) computes the cumulative probability distribution of the standard probability density ΔRR histograms. A calculator 902 computes the cumulative probability distribution of test probability density ΔRR histograms. According to the KS test, one assesses if two given distributions are different from each other. In other words, the greatest vertical distance *D* between the two cumulative probability distributions is measured by a calculator 903 which returns a *p* value in the following manner:

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$$p \equiv Q(\lambda) = 2\sum_{j=1}^{\infty}(-1)^{j-1}e^{-2j^2\lambda^2}$$

where $\lambda = (\sqrt{N_e} + 0.12 + 0.11/\sqrt{N_e}) * D.$ $N_e = \frac{N_1 N_2}{N_1 + N_2}$. N_1 is the number of data points on the standard cumulative probability distribution. N_2 is the number of data points in the test cumulative probability distribution. A detector 904 determines whether the p value is greater than a certain, appropriately selected threshold P_c, and detection of $p > P_c$ indicates that the cumulative probability distributions are not significantly different from one another. Since the standard ΔRR probability density histograms is representive of atrial fibrillation, a value of $p > P_c$ constitutes a positive identification of atrial fibrillation (or more accurately failure to reject the hypothesis that the test cumulative probability distribution is not atrial fibrillation) (208 in Figure 2).

Figures 6a and 6b show a comparison of the ΔRR probability density histograms in terms of standard deviation and skewness. A small D defined above indicates that the standard deviation and the skewness of a test ΔRR probability density histogram are clustered around those of the standard ΔRR probability density histograms.

The results were assessed by four categories as followed: true positive (TP) -- atrial fibrillation is classified as atrial fibrillation; true negative (TN) -- non-atrial fibrillation is classified as non-atrial fibrillation; false negative (FN) – atrial fibrillation is classified as non-atrial fibrillation; false positive (FP) -- non-atrial fibrillation is classified as atrial fibrillation. Sensitivity and specificity are defined by TP/(TP+FN) and TN/(TN+FP),

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respectively. The predictive value of a positive test (PV+) and the predictive value of a negative test (PV-) are defined by TP/(TP+FP) and TN/(TN+FN), respectively.

The receiver operating characteristic curve (ROC) gives the sensitivity and the specificity in the artrial fibrillation detection algorithm. Variation of the value of P_c determines the ROC. Figure 7 shows the ROC of the assessment of the KS test for the MIT-BIH atrial fibrillation/flutter database. Reducing P_c, the sensitivity increases and the specificity decreases. Assuming P_c = 0.003944, the sensitivity is 96.5%, the specificity is 96.5%, the PV+ is 95.2% and PV- is 97.5%. P_c is therefore a sensitivity-altering and specificity-altering parameter.

It will appear to those of ordinary skill in the art that the method of Figure 2 and the system of Figure 8 can be implemented through a properly programmed computer.

Although the present invention has been described hereinabove by way of a preferred embodiment thereof, this embodiment can be modified at will, within the scope of the appended claims, without departing from the spirit and nature of the subject invention.

WHAT IS CLAIMED IS:

1. A method for detecting cardiac arrhythmia of a patient, comprising:

detecting RR intervals of the patient, wherein each RR interval is an interval between two heart beats;

constructing standard histograms of ΔRRs collected during cardiac arrhythmia of a plurality of subjects, wherein each ΔRR is a difference between two successive RR intervals;

constructing test histograms of ΔRRs of the patient from the detected RR intervals of said patient; and

comparing said standard and test histograms to detect whether said patient suffers from cardiac arrhythmia.

2. A method for detecting cardiac arrhythmia as defined in claim 1, wherein the standard and test histograms are probability density histograms.

3. A method for detecting cardiac arrhythmia as defined in claim 1, further comprising calculating a mean value of a given number of successive RR intervals of the patient, and choosing one of the standard probability density histograms in relation to said mean value.

4. A method for detecting cardiac arrhythmia as defined in claim 3, wherein choosing one of the standard probability density histograms comprises selecting the standard histogram corresponding to the range of RR intervals in which said mean value is located.

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5. A method for detecting cardiac arrhythmia as defined in claim 1, wherein said comparing of the standard and test histograms comprises adjusting a specificity-altering and sensitivity-altering parameter.

6. A method for detecting cardiac arrhythmia as defined in claim 1, wherein said comparing of the standard and test histograms comprises calculating a standard cumulative probability distribution from said standard ΔRR probability density histograms, calculating a test cumulative probability distribution from said test ΔRR probability density histograms, and computing a deviation between said standard and test distributions.

7. A method for detecting cardiac arrhythmia as defined in claim 5, wherein said comparing of the standard and test histograms comprises:

calculating a standard cumulative probability distribution from said standard ΔRR probability density histograms;

calculating a test cumulative probability distribution from said test ΔRR probability density histograms;

computing a deviation between said standard and test distributions; and

detecting cardiac arrhythmia when the computed deviation is higher than said specificity-altering and sensitivity-altering parameter.

8. A system for detecting cardiac arrhythmia of a patient, comprising:

a RR interval detecting monitor detecting RR intervals of the patient, wherein each RR interval is an interval between two heart beats;

a standard ΔRR histogram storage unit in which are stored standard histograms of ΔRRs collected during cardiac arrhythmia of a

plurality of subjects, wherein each ΔRR is a difference between two successive RR intervals;

a test ΔRR histogram calculator supplied with the detected RR intervals from the monitor and constructing test histograms of said ΔRRs of said patient; and

a standard and test ΔRR histograms comparator supplied with said standard and test histograms, said comparator comprising a detector of cardiac arrhythmia of the patient responsive to the comparison of said standard and test histograms.

9. A system for detecting cardiac arrhythmia as defined in claim 8, wherein the standard and test histograms are probability density histograms.

10. A system for detecting cardiac arrhythmia as defined in claim 8, further comprising a calculator of a mean value of a given number of successive RR intervals of the patient, and a selector of one of the standard probability density histograms in relation to said mean value.

11. A system for detecting cardiac arrhythmia as defined in claim 10, wherein the selector of one of the standard probability density histograms comprises means for selecting the standard histogram corresponding to the range of RR intervals in which said mean value is located.

12. A system for detecting cardiac arrhythmia as defined in claim 8, wherein said standard and test ΔRR histograms comparator comprises an adjustable, specificity-altering and sensitivity-altering parameter.

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13. A system for detecting cardiac arrhythmia as defined in claim 8, wherein said standard and test ΔRR histograms comparator comprises a calculator of a standard cumulative probability distribution from said standard ΔRR probability density histograms, a calculator of a test cumulative probability distribution from said test ΔRR probability density histograms, and a calculator of a deviation between said standard and test distributions.

14. A method for detecting cardiac arrhythmia as defined in claim 12, wherein the standard and test ΔRR histograms comparator comprises:

a calculator of a standard cumulative probability distribution from said standard ΔRR probability density histograms;

a calculator of a test cumulative probability distribution from said test ΔRR probability density histograms;

a calculator of a deviation between said standard and test distributions; and

a detector of a cardiac arrhythmia when the computed deviation is higher than said specificity-altering and sensitivity-altering parameter.

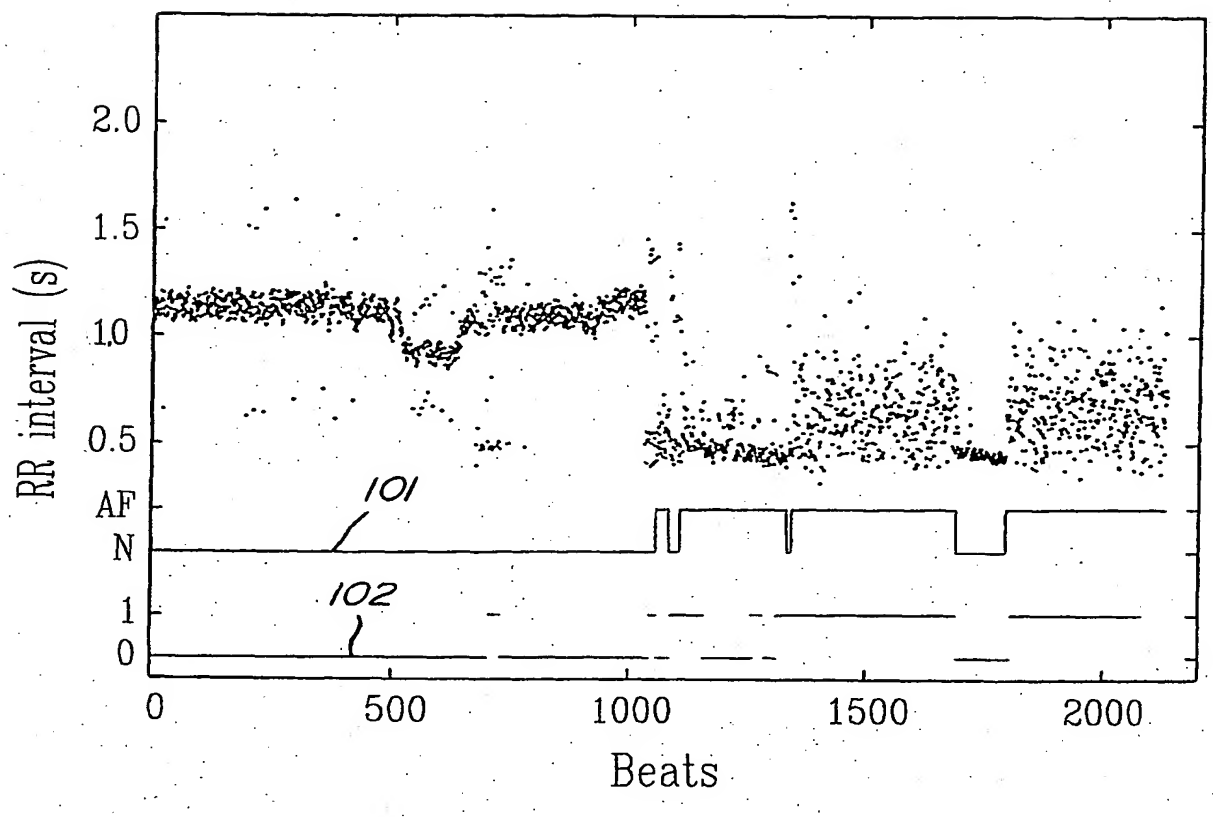

FIG. 1

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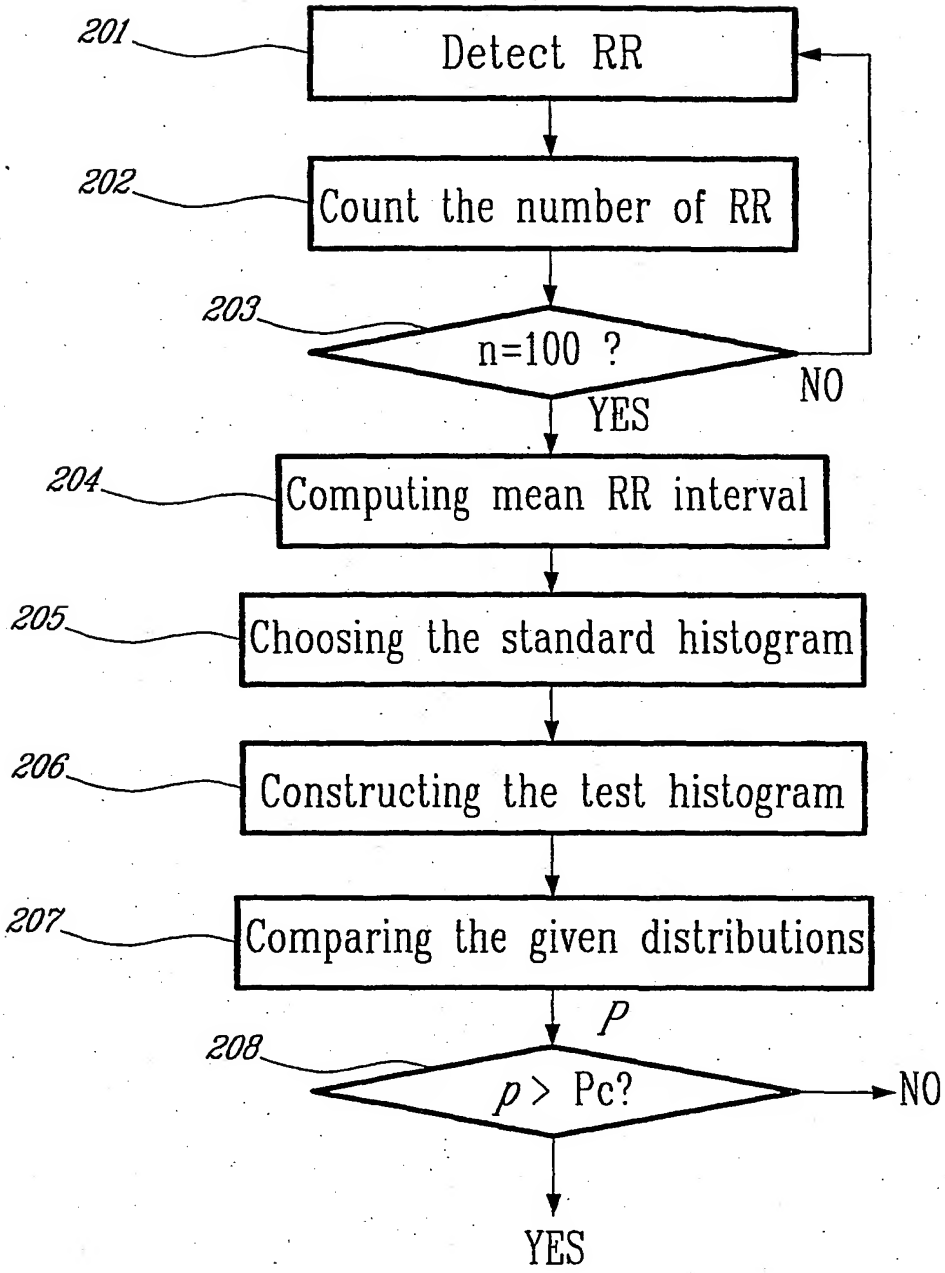

FIG. 2

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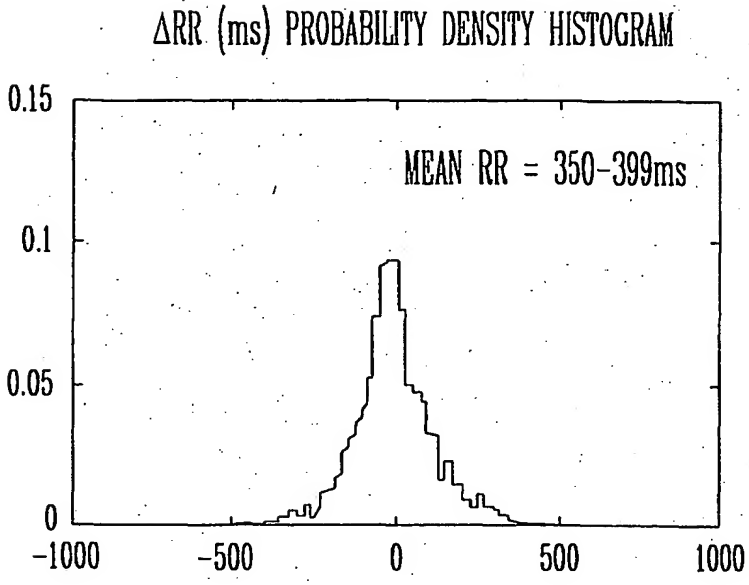

FIG_3a

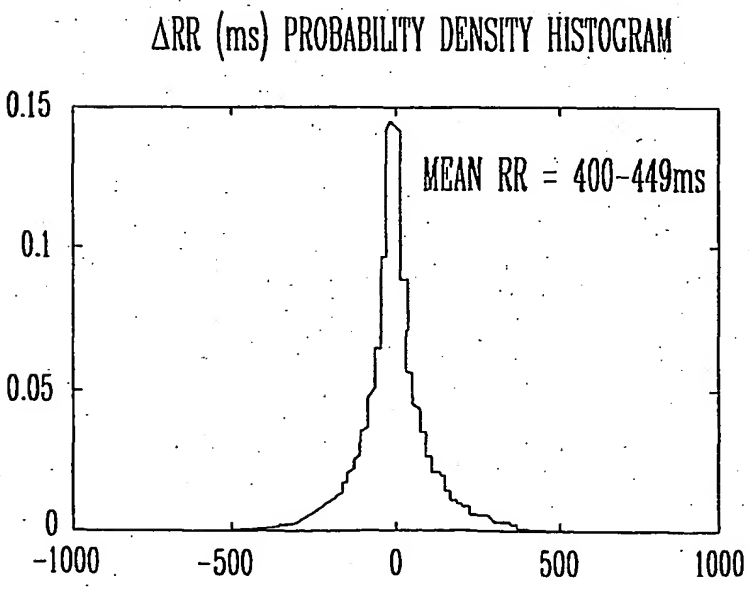

FIG_3b

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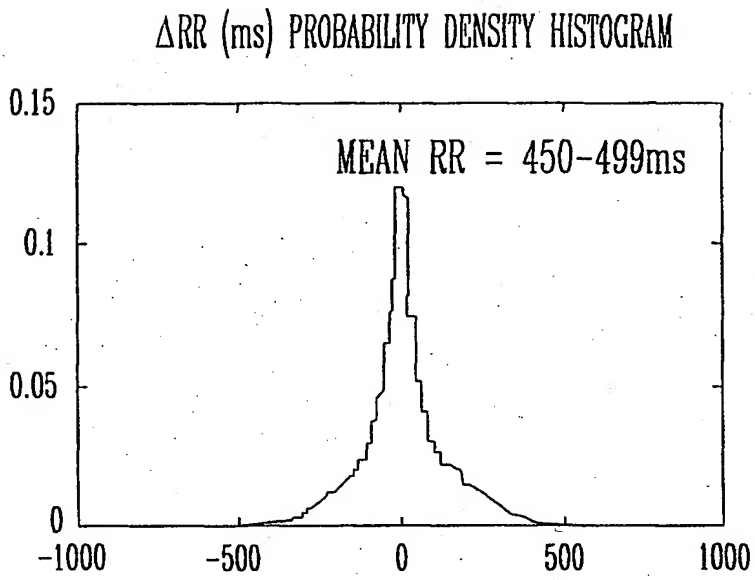

FIG_3c

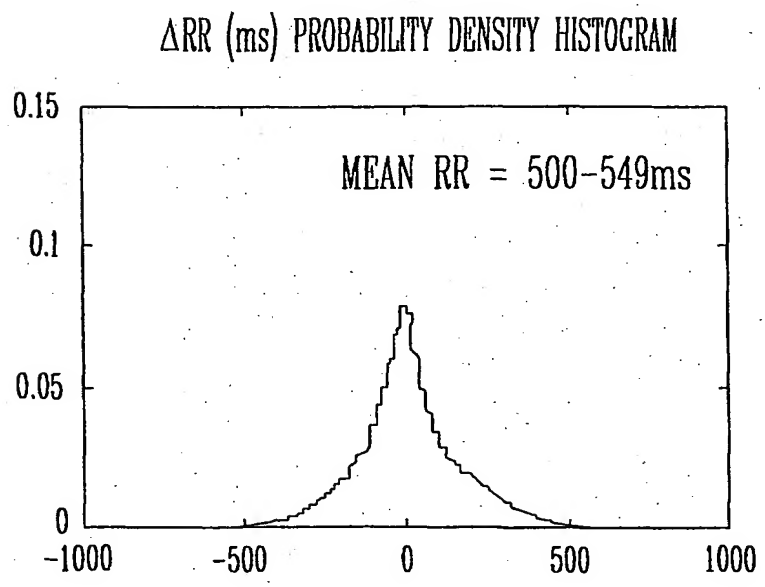

FIG_3d

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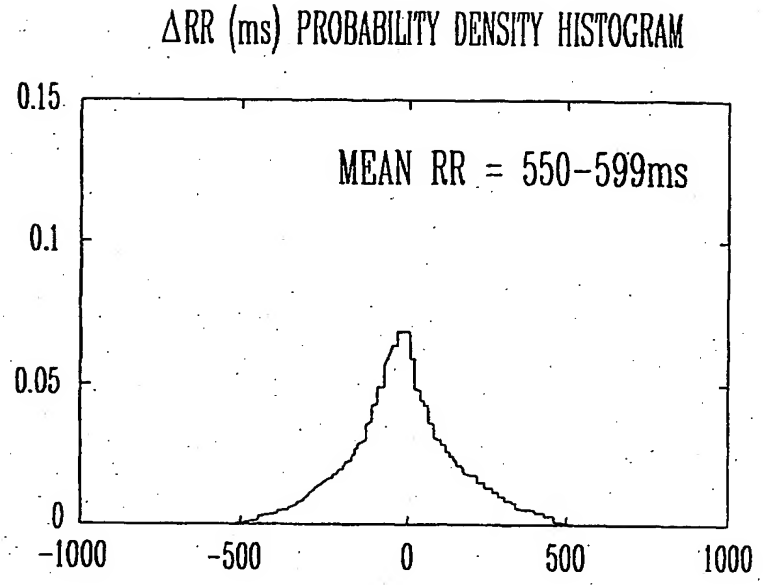

FIG_3E

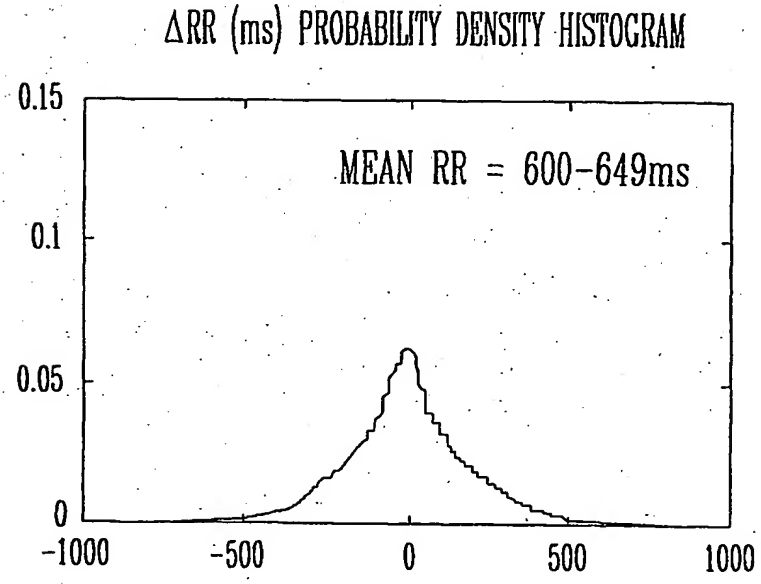

FIG_3F

SDOCID: <WO___0224068A1_I_>

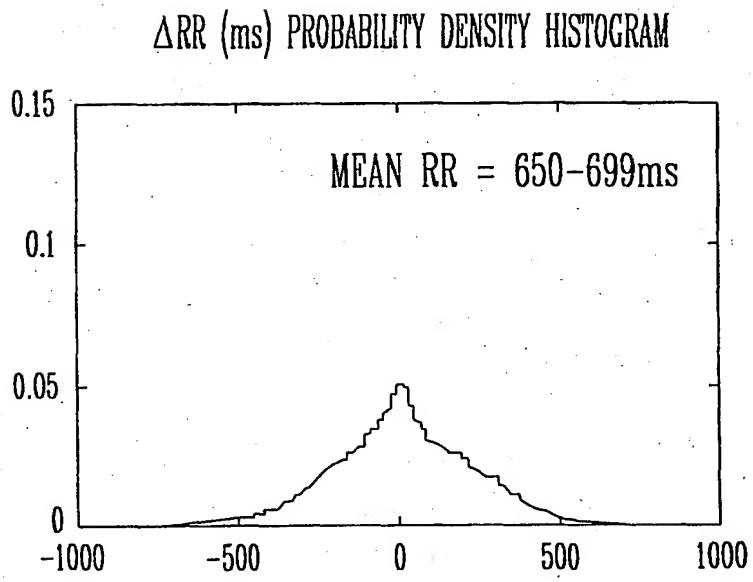

FIG. 3g

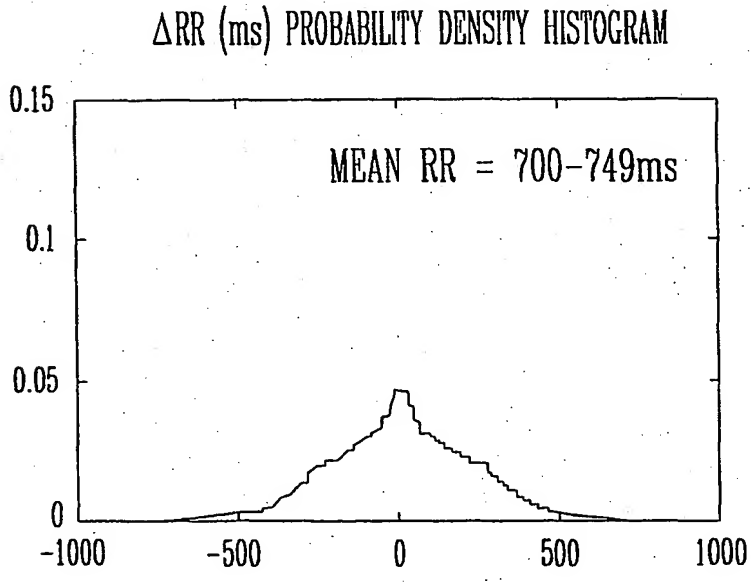

FIG. 3h

NSDOCID: <WO___0224068A1_I_>

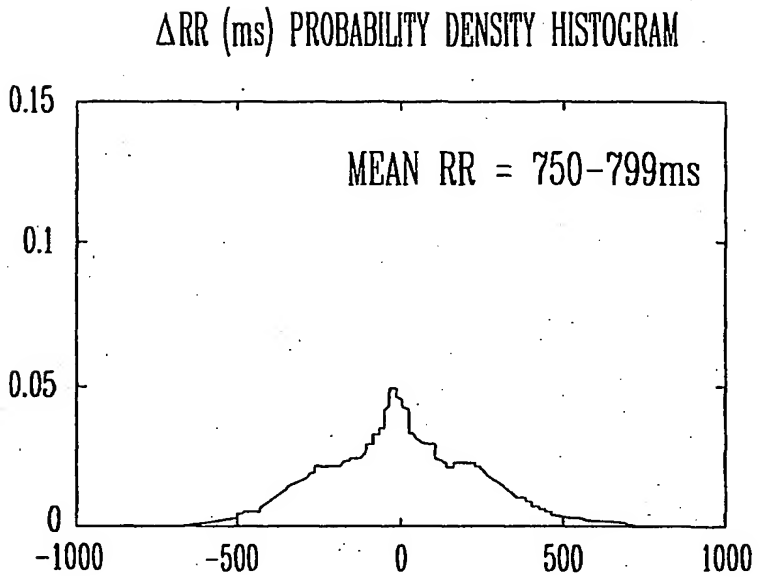

FIG. 3i

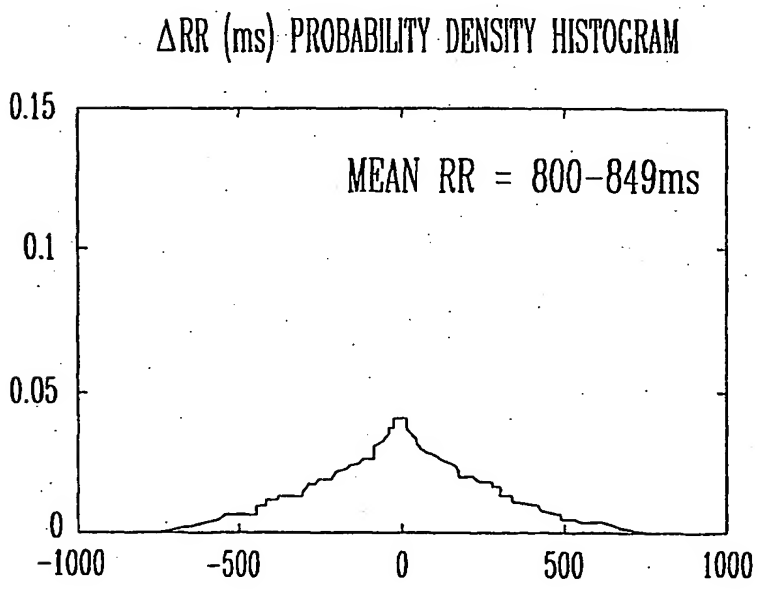

FIG. 3j

SDOCID: <WO___0224068A1_I_>

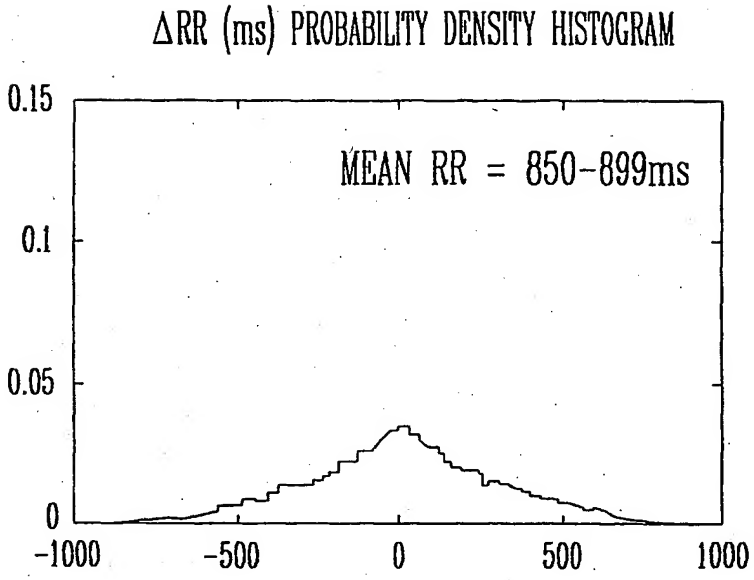

Fig. 3K

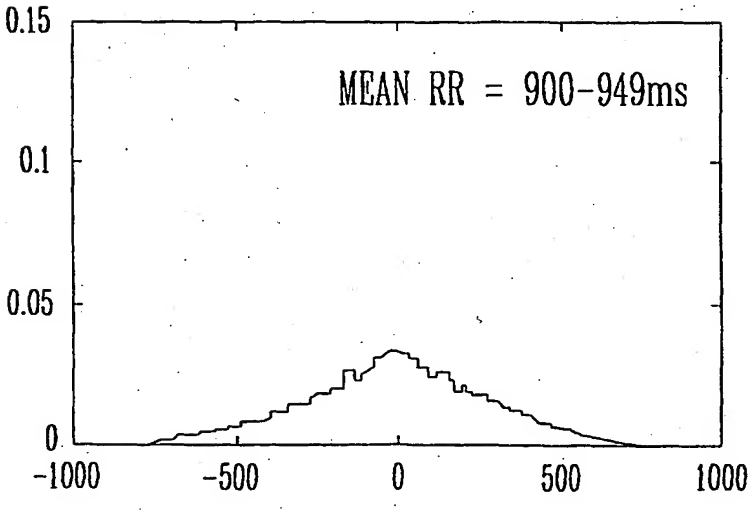

Fig. 3L

ISDOCID: <WO___0224068A1_I_>

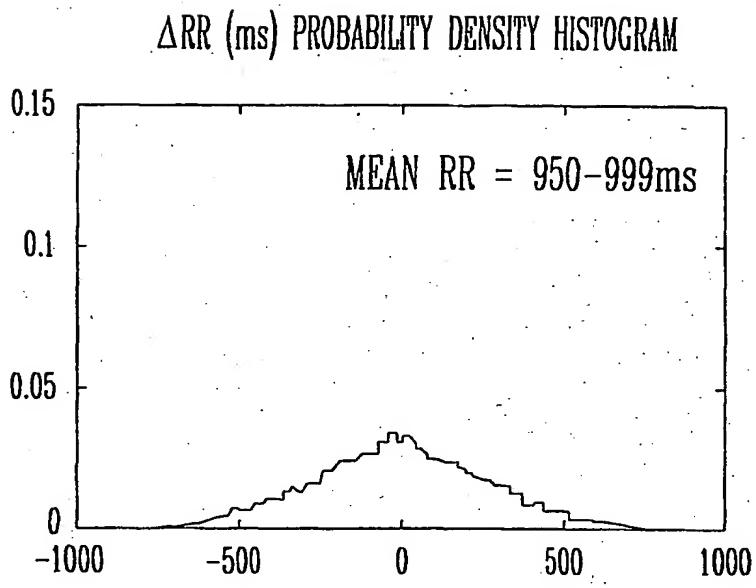

FIG_3M

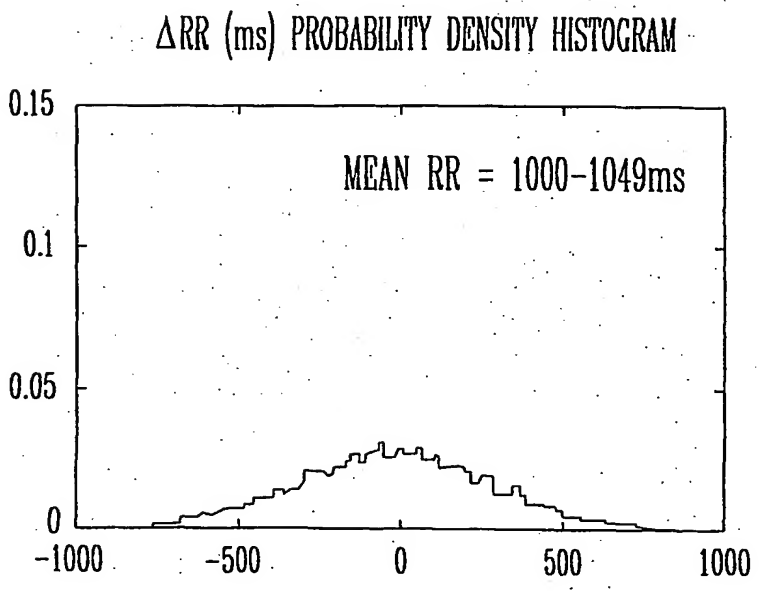

FIG_3N

DOCID: <WO___0224068A1_I_>

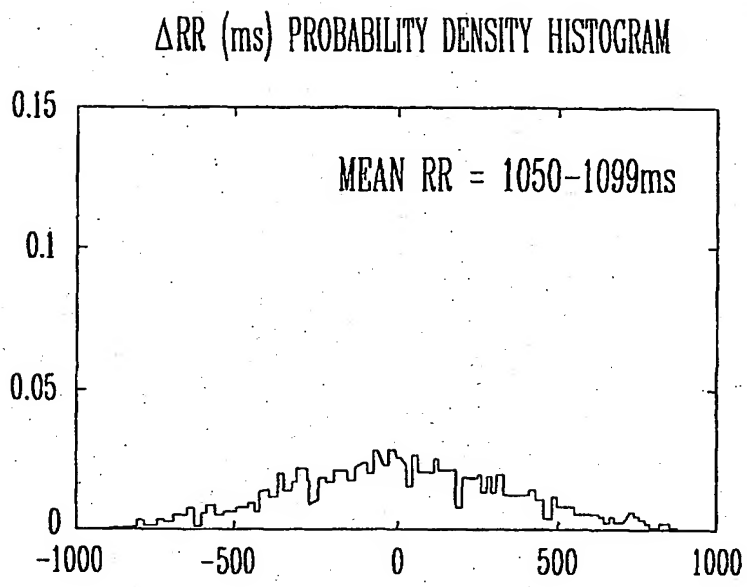

FIG_3D

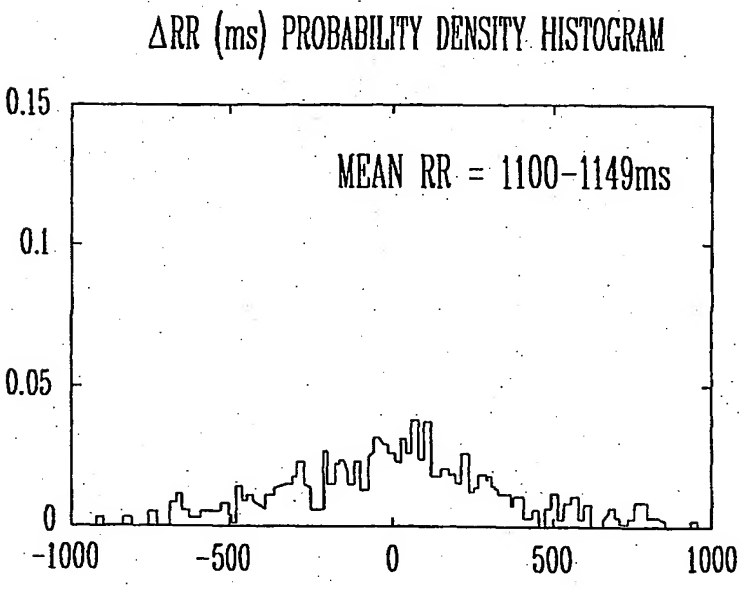

FIG_3P

ISDOCID: <WO___0224068A1_I_>

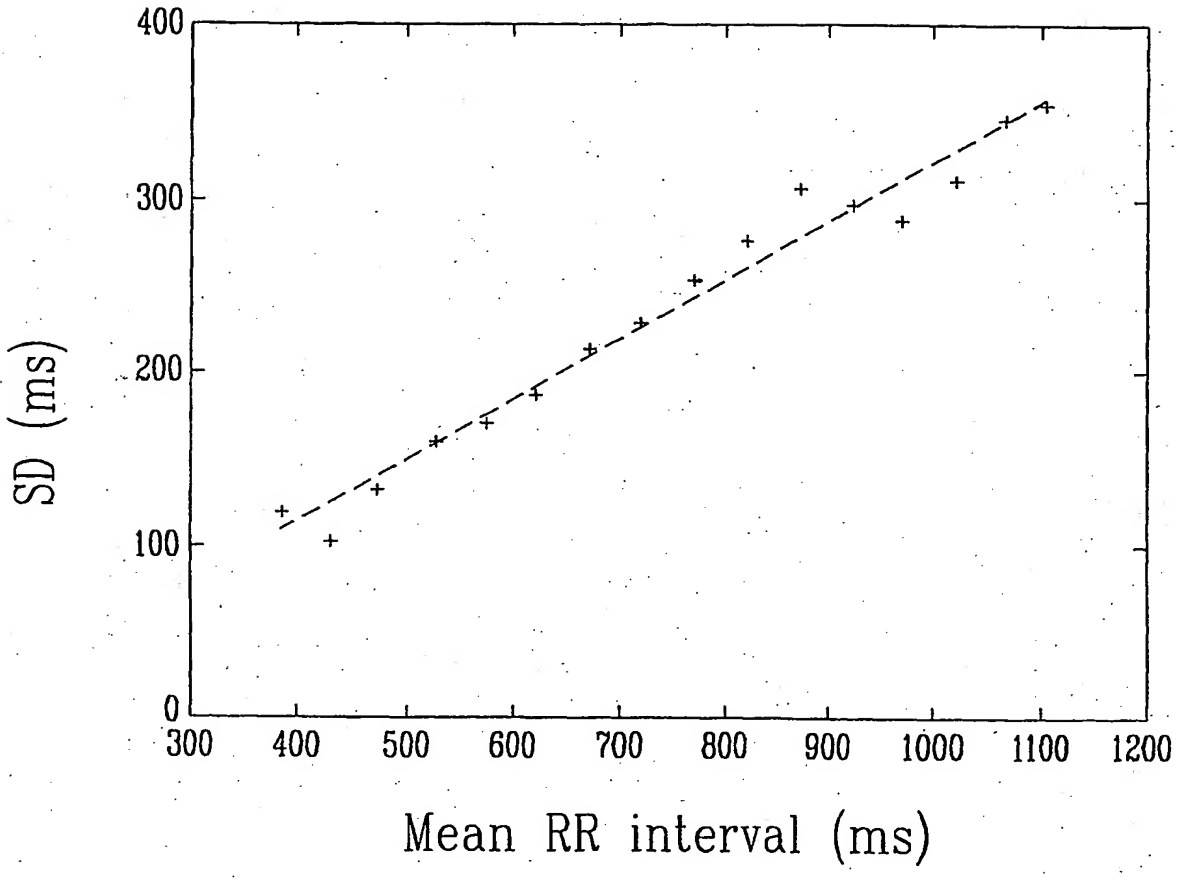

FIG_4

SDOCID: <WO___0224068A1_I_>

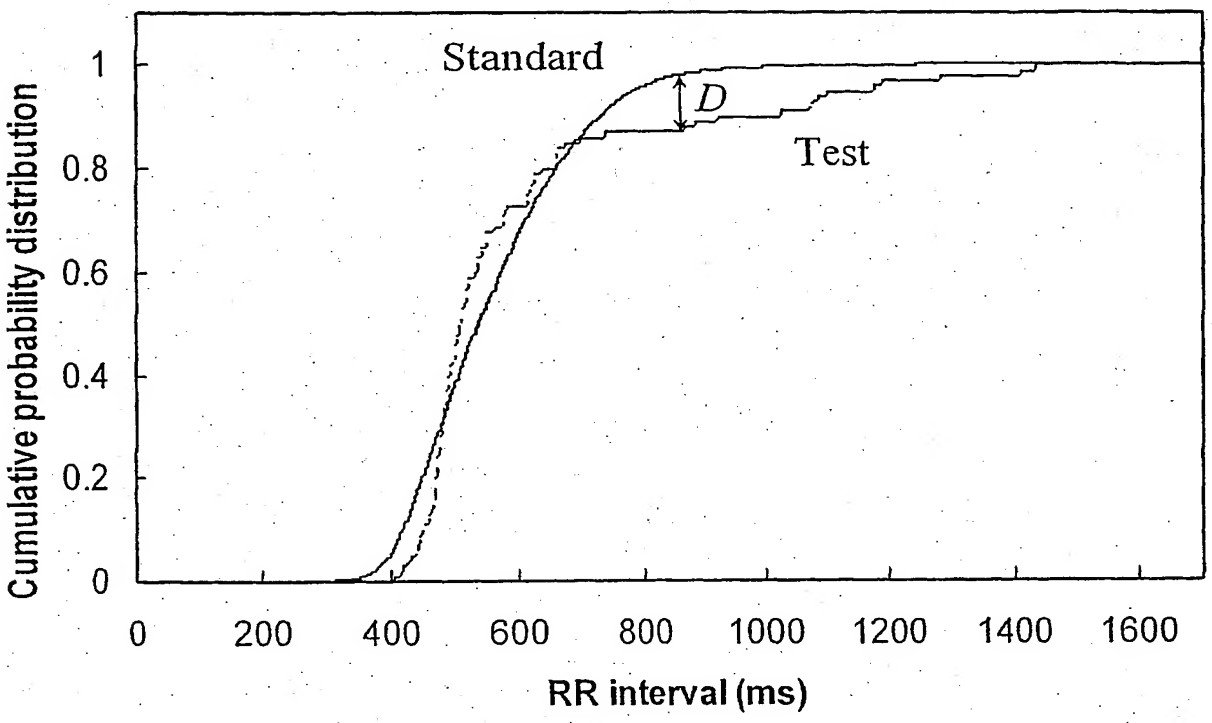

FIG_5

ISDOCID <WO__ 0224068A1 I >

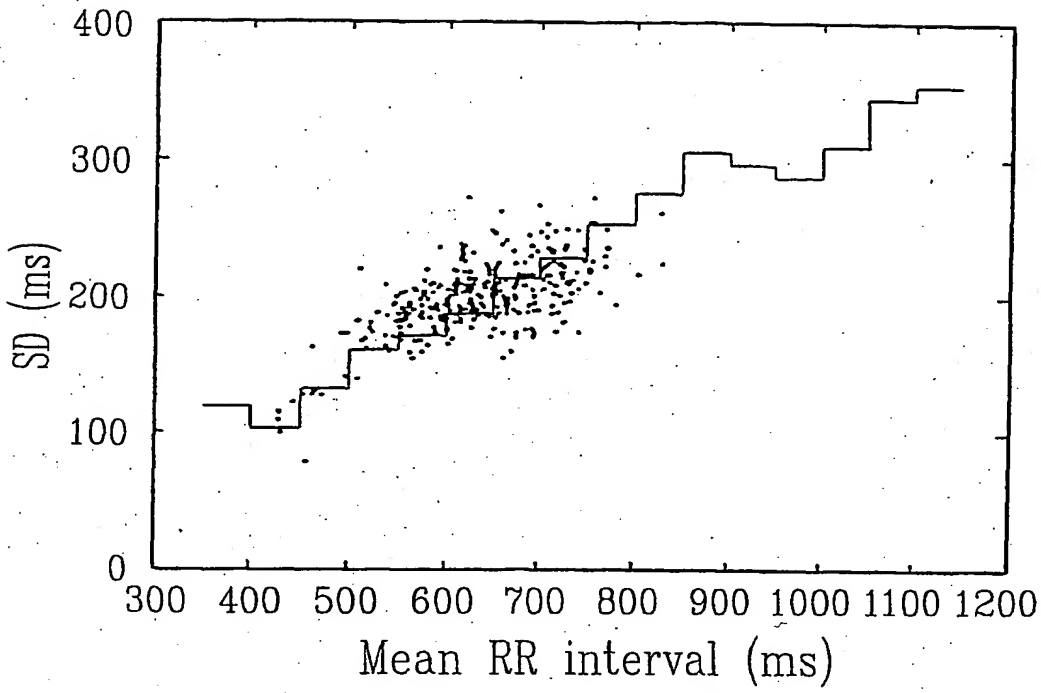

Fig. 6a

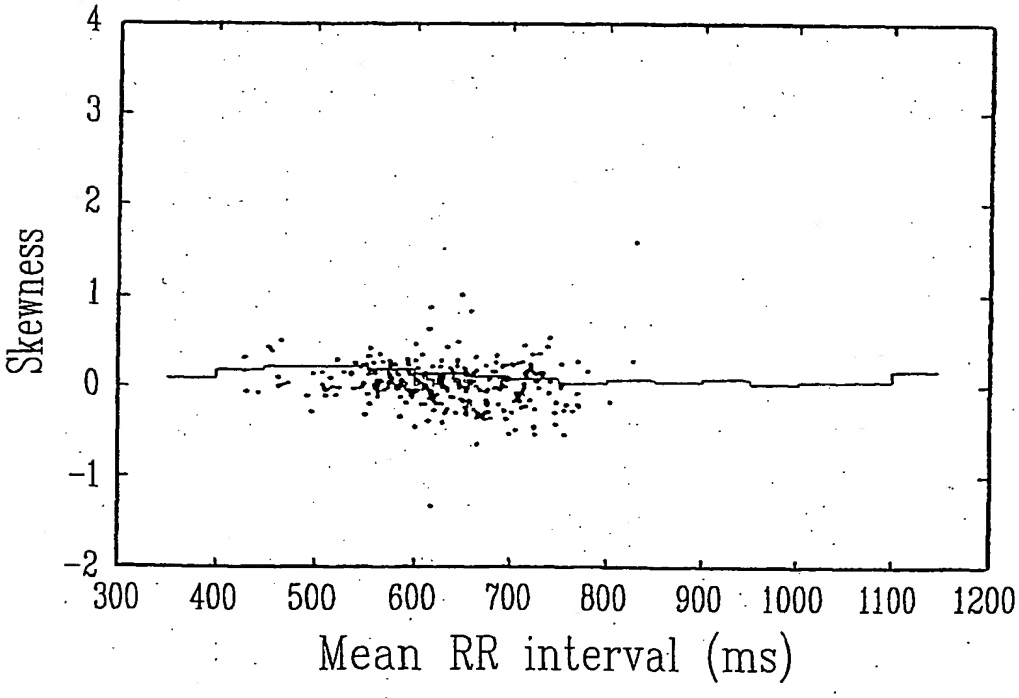

Fig. 6b

SDOCID: <WO___0224068A1_I_>

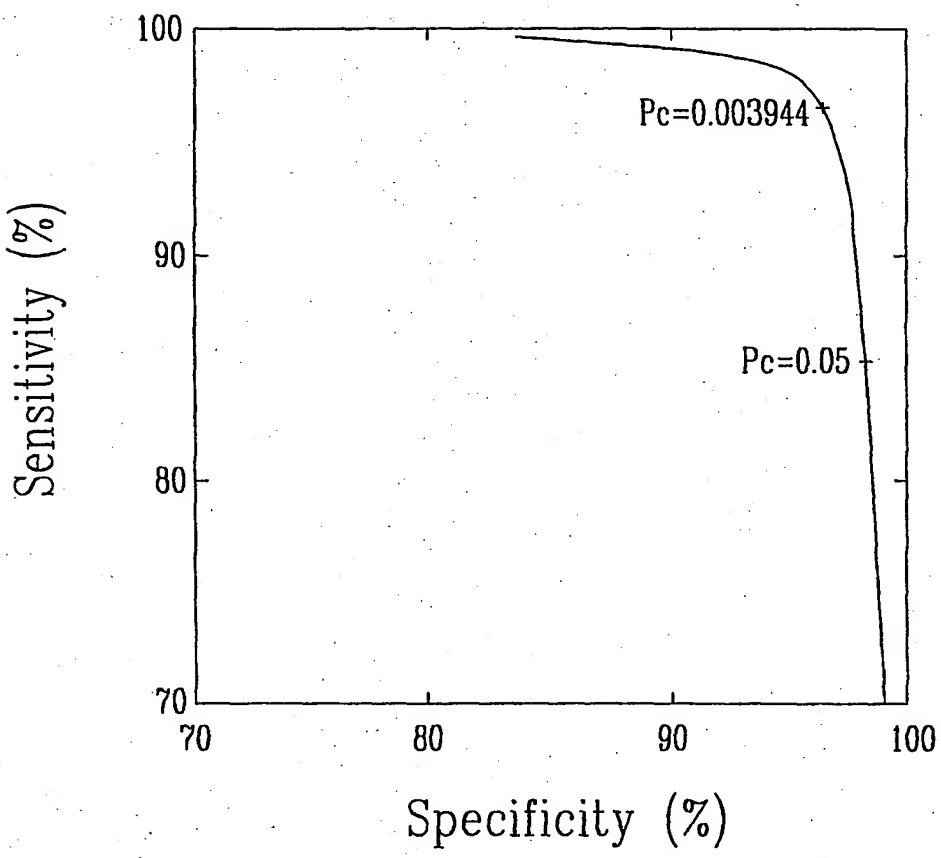

FIG_7

SDOCID <WO 0224068A1 I >

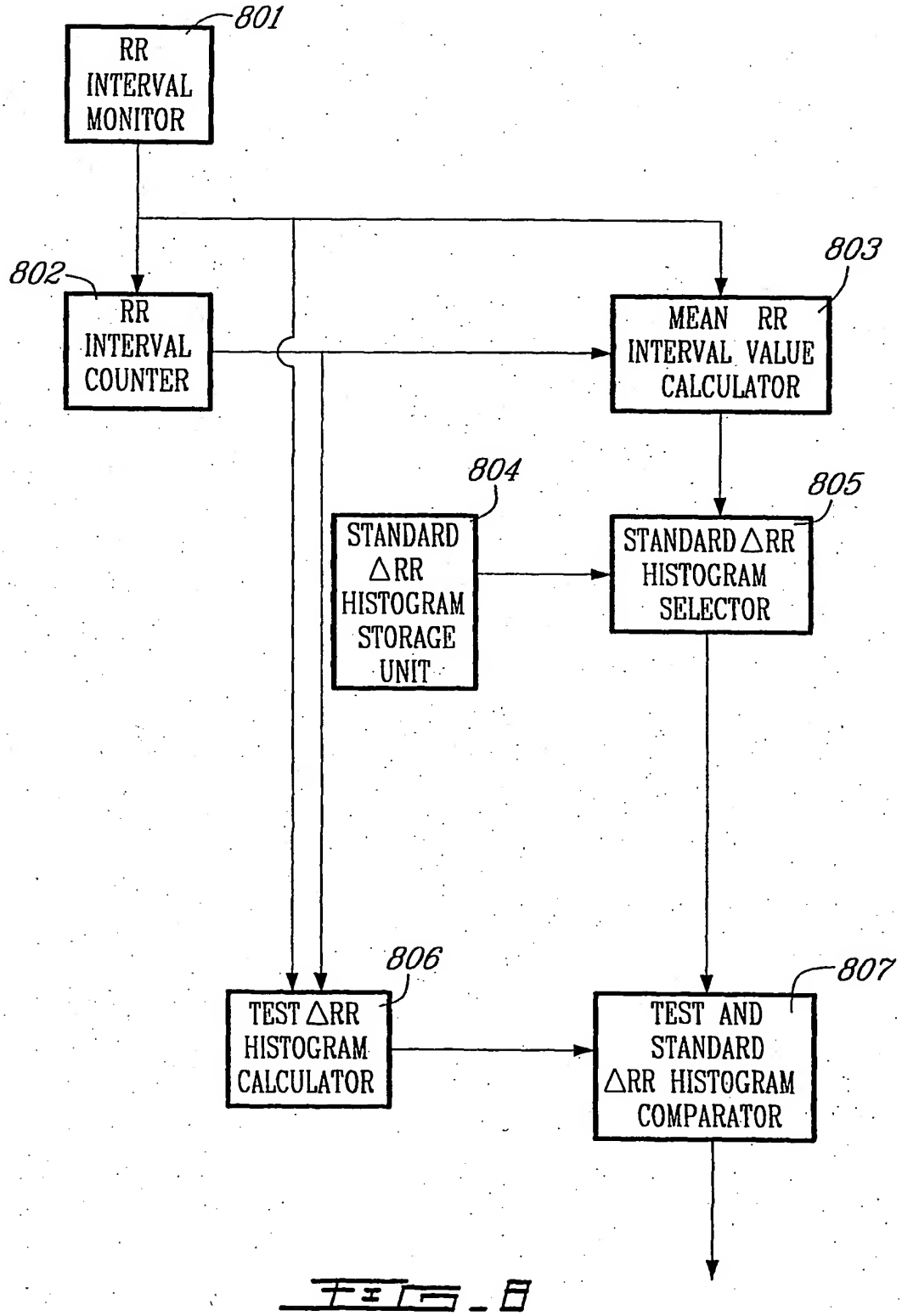

Fig. 8

SDOCID: <WO___0224068A1_I_>

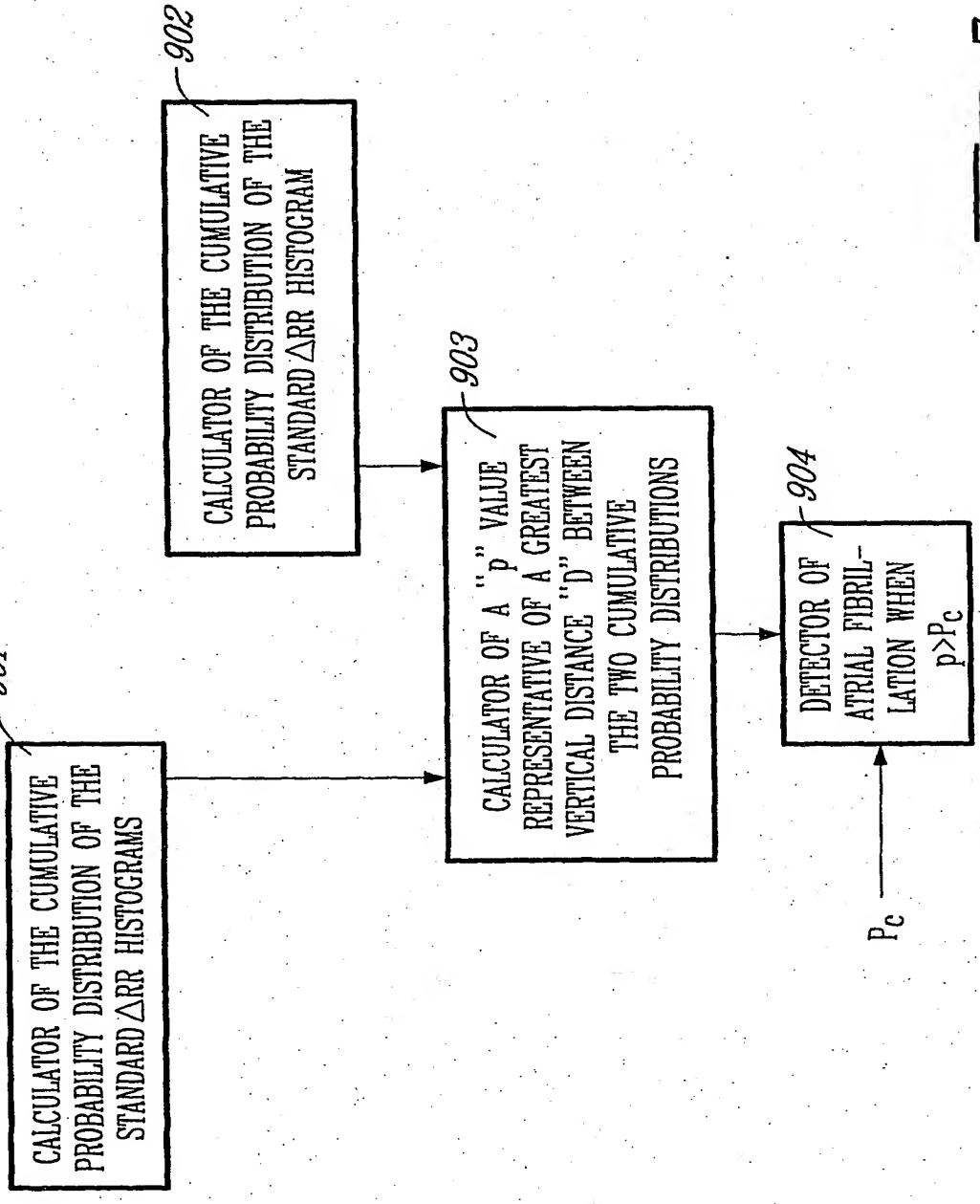

FIG. 9

\SDOCID: <WO___0224068A1_I_>

TERNATIONAL SEARCH REPORT

national Application No
PCT/CA 01/01360

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B5/046 A61N1/37 G06F17/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B A61N G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 603 331 A (CARLSON GERRARD M ET AL) 18 February 1997 (1997-02-18) column 2, line 43 -column 3, line 8 column 3, line 40 - line 47	1-4,8-11

[ ] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
19 February 2002	26/02/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Martelli, L

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TERNATIONAL SEARCH REPORT

Information on patent family members

National Application No
PCT/CA 01/01360

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5603331 A	18-02-1997	NONE	

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